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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/799,284	03/12/2004	Rob Barber	674523-2033	8663

20999 7590 12/15/2005

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EXAMINER	
MCGILLEM, LAURA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/799,284	BARBER ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Oath/Declaration

Applicant has not given a post office address anywhere in the application papers as required by 37 CFR 1.33(a), which was in effect at the time of filing of the oath or declaration. A statement over applicant's signature providing a complete post office address is required.

Priority

It is noted that this application is a continuation-in-part of International application No. PCT/GB02/04169, filed on Sep. 12, 2002 and receives priority to Great Britain Application Nos. 0122237.1, filed on 9/14/2001 and 0210575.7, filed on 9/8/2002.

Specification

The abstract of the disclosure is objected to because it contains the acronyms EOI and DRG and it is not immediately obvious what the acronyms are intended to represent. It would be remedial to include the entire phrase along with the acronym. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation *United States v. Telectronics*, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Scope of the claims. The invention is drawn to a method for treating or preventing pain in a subject, including a human subject by administering a lentiviral vector system comprising an entity of interest (EOI), an EOI to treat or prevent pain and a method to identify or validate an (EOI) useful to prevent or treat pain. The scope of the claims is extremely broad because it encompasses a very large group of pain types, including all types of acute pain (i.e. a stab wound or headache, for example), or chronic pain resulting from any type of disease such as cancer or diabetes. The scope of the claims encompasses prevention (i.e. to keep from happening or existing) of pain, which includes preventing unanticipated pain. The claims are drawn to an entity of interest to treat or prevent pain which encompasses an extremely large number of entities

including any chemical compound, biological compound or combinations thereof such as a protein, a nucleotide sequence, an organic and/or an inorganic pharmaceutical (such as an analgesic, an anti-inflammatory, a hormone, a lipid), or combinations thereof (see specification paragraph 0180).

2) Unpredictability of the art. The art regarding the treatment and prevention of pain with lentiviral vectors administered to the nervous system is unpredictable, manifested in multiple issues related to the use of lentiviral vectors in humans. Thomas et al (Nat. Gen. 2003, Vol. 4, pp. 346-358) teach that lentiviral vectors are effective for gene delivery to non-dividing cells of the central nervous system (see page 348, right column, 2nd full paragraph). However, Thomas et al also teach that multiple safety issues such as potential immunogenicity, delivery specificity and potential for insertional mutation of oncogenes are a concern when using lentiviral vectors for human gene therapy applications. Thomas et al teach that although lentiviral vectors themselves show low immunogenicity, there is potential for an immune response against the expressed product delivered by the vector (see page 353, right column, 3rd full paragraph). Therefore, the immune response against any number of entities of interest (EOI) delivered to the DRG by a lentiviral vector is unpredictable. An additional concern is the unpredictability that a promiscuous viral vector and the expressed protein will remain in the targeted cells or tissues, which may result in detrimental effects to healthy cells or tissue, especially in the case of lentiviral vectors which can cross the nuclear membrane (see page 354, left column, 1st full paragraph). A third safety issue regarding the use of chromosomally integrating viral delivery systems relates to the possibility of

integration of the delivered gene of interest into a potential oncogene, known as insertional mutagenesis. Thomas et al describe a recent rodent trial involving retroviral-based gene therapy, which unexpectedly resulted in leukemia due to viral integration into a myeloid leukemia-related transcription factor (see page 355, left column, paragraphs 1 and 2, for example). Thomas et al conclude that multiple hurdles regarding the safety of integrating viral vectors remain, including limited understanding of integration potential into potential oncogenes, potential for immune response and the ability of animal studies to predict response in humans.

3) State of the Art. In a recent post-filing review, G. Romano (Drug News Perspective, 2005, Vol. 18 (2). Pp. 128-134) teaches that the lentiviral vector family includes HIV-1 derived vectors, as well as multiple non-HIV-1-derived vectors, and that the multiple safety issues regarding the use of HIV-1 derived vectors requires improvement of non-HIV derived vectors (see page 128, summary and right column). Although Romano teaches that the eight non-HIV-1-derived vectors are safer than HIV vectors, Romano also teaches that all of the other viruses have the potential for insertional mutagenesis and for formation of replication compentent viruses due to unexpected homologous recombination events (see Table 1, Page 130). Fink et al (Adv. Drug Del. Rev. 2003, Vol. 55, pp 1055-2064) teaches that pain can potentially be alleviated by administration of bioactive substances into nerve cells involved in the pain processing pathway by adenoviral or herpes simplex virus (HSV)-based transfer of genes encoding proteins that are subsequently delivered to the cell body via retrograde transport (see page 1058, right column, 2nd paragraph, for example). For example,

direct injection of an HSV vector comprising a protein involved in multiple pain types did result in a localized temporary analgesic effect in rodent models (see page 1059, right column, for example). Despite success in animal models, Fink et al teach that due to the complexity of central nervous system function, application of viral vector-based pain analgesia to human clinical trials requires further development. Thomas et al disclose that since human responses to viral-based therapies are more variable than those observed in animal models, it is difficult to make solid predictions based on preclinical trials (see page 356, left column, 1st full paragraph).

4) Amount of guidance provided. Applicants have not provided any guidance regarding what particular EOI (DNA, RNA, proteins or drugs) other than a potassium ion channel, a sodium channel protein or a calcium sensing protein can be used to treat or prevent pain. Applicants have not addressed art-recognized issues with regard to safety, inflammation, and oncogenic potential of viral vectors. Applicants have not addressed which type of *in vivo* model for pain will be used to select an EOI with therapeutic potential. Applicants have provided no guidance on efficacy of said treatment for any pain with any number of variable manifestations, including area of the pain, severity of the pain and patient population. Applicants have not provided guidance on administration of the composition such as dosages, number of times treatment is necessary or duration of treatment. Applicants have not provided any guidance on how pain can be prevented in a subject by administering an EOI to the dorsal root ganglion (DRG) with a lentiviral vector system. Applicants have not provided guidance on effective dosages of any EOI used to prevent pain or number of treatments necessary

to prevent pain. The specification does not provide information on length of treatment with an EOI which is effective to prevent pain. Applicants have not provided any guidance on how to predict when pain will occur, in order to determine the appropriate time to administer an EOI to the subject's DRG with a lentiviral vector system. It is clear that the skilled artisan would have had to have practiced trial and error experimentation in order to practice the claimed invention.

5) Working examples. Applicants provide examples of introduction of a reporter protein via a viral vector *in vitro*, and an *in vivo* rodent model by direct injection, peripheral administration and spinal cord injection. Applicants provide examples of introduction of a potassium channel and a sodium channel protein via the same methods. Applicants exemplify a method to screen test compounds by expressing a calcium sensing protein or an ERK signaling activator and comparing RNA expression in response to physiological signals associated with modulation of pain. While Applicants have successfully demonstrated that various proteins *associated* with modulation of pain (as well as a multitude of other signaling cascades) can be delivered into cells via viral vectors by the claimed methods, Applicants have not actually exemplified treatment or prevention of pain using any of these models. Applicants have provided no working examples of an EOI effective to prevent pain. Applicants have not provided examples of a method of identification or validation of an EOI useful to prevent pain.

6) Nature of the invention. The invention involves one of the most complex, unpredictable and controversial aspects of science and medicine to date, the use of gene therapy for treatment or prevention of pain.

7) Level of skill in the art. The level of skill in the art is very low because the Applicants have not reduced to practice the claimed methods of treating or preventing pain.

Given the above analysis of the factors which the Courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have practiced undue and excessive experimentation in order to practice the claimed invention.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation *United States v. Telectronics*, Inc., 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:

1) Scope of the claims. The claimed invention reads on a method for the identification and validation of an EOI useful in the prevention or treatment of pain by delivering a test EOI to a target cell wherein the target cell is *in vitro* and analyzing the effect of the EOI on a target cell in order to select an EOI with therapeutic potential for prevention or treatment of pain. Therefore the claim reads on an ***in vitro*** method to identify an entity for treatment of pain, which is an extremely complex process involving the sensory nervous system of a multicellular organism.

2) State of the art. Sherwood (Human Physiology: from Cells to Systems, 2nd Ed. 1989. Minneapolis) teach that the pain pathway is extremely complex involving the higher brain, brain stem, spinal cord, neurons and multiple types of pain receptors (see pages 157-159 and Figure 6-8, for example). Marban et al (WO 00/18903, of record) teach that delivery of transgenes coding for ion channels can effect cellular excitability in neurons and teach that genetic manipulation of neuronal excitability has the potential for genetic analgesia for treatment of pain (see page 2, lines 13-19 and page 10, lines 19-21), but appears to make the conclusion based on changes in the electrical excitability of the cell and does not actually treat pain *in vitro*.

3) Unpredictability of the art. Based on the complexity of the pain pathway both anatomically and biochemically, it is extremely unpredictable whether an EOI that treats or prevents pain would be identified or accurately validated using an *in vitro* target cell, even if the target cell is a cultured dorsal root ganglion. In a recent review of potential models for *in vitro* skin irritation and pain, Welss et al (Toxicology in Vitro, 2004. Vol.18, pp.231-243) discloses that current models do not have sufficient predictive ability

necessary to substitute for *in vivo* irritation and pain studies (see page 240, right column, in particular).

4) Amount of guidance provided. Applicants have not provided any guidance on how to evaluate pain in an *in vitro* target cell, which lacks a central nervous system for the perception of pain. Applicants have not provided any guidance on how to determine if an *in vitro* target cell has been therapeutically treated for pain, (i.e. if the target cell feels relief from pain).

5) Working examples. Applicants have demonstrated that various proteins associated with modulation of pain (as well as a multitude of other signaling cascades) can be delivered into cells *in vitro* which then display altered resting membrane potentials [see paragraph 0325]; however, Applicants have not actually exemplified treatment or prevention of pain *in vitro*. Applicants have provided no working examples of an EOI effective to prevent pain identified by *in vitro* methods. Applicants have not provided examples of a method of identification or validation of an EOI useful to prevent pain *in vitro.*

6) Nature of the invention. The invention involves an extremely complex process of pain, and its treatment and prevention using methods in an *in vitro* model.

7) Level of skill in the art. The level of skill in the art is very low because the Applicants have not reduced to practice the claimed methods of identifying an entity to treating or preventing pain wherein the target cell is *in vitro*.

Given the above analysis of the factors which the Courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered

that the skilled artisan would have had to have practiced undue and excessive experimentation in order to practice the claimed invention.

Claims 16-18 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for identification or validation of an EOI for treatment or pain *in vivo*, does not reasonably provide enablement for methods for identification or validation of an EOI for treatment or pain *in vitro*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed method is drawn to the identification and validation of an EOI useful in the prevention or treatment of pain by delivering a test EOI to a target cell wherein the target cell is *in vitro* or *in vivo,* and analyzing the effect of the EOI on a target cell in order to select an EOI with therapeutic potential for prevention or treatment of pain. Analysis of the effect of the EOI can be performed by monitoring EOI-induced modulation of a transcriptome or proteasome of the target cell. The target cell can be derived from a dorsal root ganglion cell. Claim 24 is drawn to an EOI useful to treat pain that has been identified by the *in vivo* or *in vitro* method. The claims read on an *in vitro* method to identify an entity for treatment of pain, which is an extremely complex process involving the sensory nervous system of a multicellular organism. The claimed methods for identification or validation of an EOI for treatment or pain *in vitro* are not enabled for reasons discussed in the above rejection of enablement of *in vitro* methods for identifying agents to treat or prevent pain.

Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. In the instant case, the specification discloses one Rabies G protein. There is no description of mutational sites which naturally occur in the molecule and there is no description of how the structure of the disclosed Rabies G protein relates to the structure of the mutants, variants, homologues and fragments. The genus would be expected to have divergent functional properties as small changes in nucleotide sequence can have significant effects on the structure and properties of proteins. The applicant does not provide an indication of how the structure of one Rabies G protein is representative of mutants, variants, homologues and fragments. The instant specification describes preferable embodiments of what constitutes a mutant, variant, homologue or fragment of a protein (see paragraphs 0157-0175); however, a specific definition of mutants, variants, homologues and fragments of Rabies G that would effectively function in the lentiviral vector system to allow travel by retrograde transport

in a dorsal root ganglion cell is not given. The identifying attributes of the Rabies G protein that are mutants, variants, homologues and fragments to the disclosed protein that would contribute to the claimed function are not described. According to these facts, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variant of the genus and is insufficient to support them.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is vague and indefinite because it recites a cell "derived from" a dorsal root ganglion and the metes and bounds of how a cell can be derived from a dorsal root ganglion are not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16 and 20-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Goss et al (of record).

Claim 16 is drawn to a method to identify or validate an entity of interest useful in the prevention or treatment of pain. Claim 16 does not recite that a lentiviral vector system is necessary for the claimed method.

Goss et al teach a method to determine whether an opioid peptide known as enkephalin has an antinociceptive effect in a rodent model. Goss et al teach that a viral vector encoding a human gene for proenkephalin or a viral vector encoding a reporter gene only were injected subcutaneously to the rear paws of a rat model (see page 554, right column, 3rd paragraph, and page 555, left column, for example). A subset of the control and experimental rat population were sacrificed, the DRG was removed and analyzed for presence of proenkephalin DNA (see page 555, left column 3rd paragraph and page 552, Figure 2, for example) which reads on delivering a test entity of interest (EOI) to a DRG of a subject or *in situ* within the DRG of the subject. Evaluation of the effect of proenkephalin on pain relief as compared to control was performed with the formalin footpad test, in which rats were observed for a period of time after formalin injection and pain related behavior was rated by assigning a weighted pain score (see page 555, left column, last paragraph, for example which reads on analyzing pain in a subject and analyzing the reception of pain in a subject. Goss et al conclude that proenkephalin delivered in a viral vector to DRG of rats produces a pain relieving effect

over control viral vectors (se page 554, right column, 1st full paragraph for example) which reads on identifying and validating an EOI useful in the treatment of pain, and reads on an EOI useful in the treatment of pain identified by the method described above.

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 6,677,332 (Cuny et al).

Cuny et al teach therapeutic compounds that are ligands for G-protein-coupled or opioid cellular receptors wherein the selectivity of said ligand renders the ligand an effective therapeutic agent for pain that is due to the biochemical or physiological processes associated with those receptors (see column 31, lines 52-65, column 32, column 32, lines 1-9, 21-25, 49-55) which reads on an EOI useful in the prevention or treatment of pain delivered to a target cell (i.e. which is comprised of a G-protein-coupled or opioid cellular receptor). Cuny et al teach that analgesic or pain relief effects of compounds can be analyzed in an *in vivo* rodent model by administering a compound and performing the "tail flick" test. Cuny et al teach that the analgesic effect of the compound can be determined by noting whether or not there is an increase in time from administration of a noxious thermal stimulus to the occurrence of a tail flick in response to the stimulus (see column 39, lines 25-35, for example), which reads on a method to identify an EOI useful in the treatment or prevention of pain comprising delivering a test EOI to a target cell, analyzing the effect of the EOI of the target cell and selecting an EOI with therapeutic potential.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,677,332 (Cuny et al) in view of U.S. Patent No. 6,221,600 (MacLeod et al).

Applicants claim a method to identify an EOI useful in the treatment or prevention of pain comprising delivering a test EOI to a target cell, analyzing the effect of the EOI of the target cell by monitoring EOI-induced modulation of a transcriptome of the target cell and selecting an EOI with therapeutic potential.

As described in the above rejection, Cuny et al teach therapeutic compounds that are ligands for G-protein-coupled or opioid cellular receptors wherein the selectivity of said ligand renders it an effective therapeutic agent for pain that is due to the physiological processes associated with those receptors (see column 31, lines 52-65, column 32, column 32, lines 1-9, 21-25, 49-55) which reads on an EOI useful in the prevention or treatment of pain delivered to a target cell (i.e. which is comprised of a G-protein-coupled or opioid cellular receptor). Cuny et al teach that analgesic or pain relief effects of compounds can be analyzed in an *in vivo* rodent model by administering a compound and performing the "tail flick" test. Cuny et al teach that the analgesic effect of the compound can be determined by noting whether or not there is an increase in

time to the occurrence of a tail flick in response to a noxious thermal stimulus (see column 39, lines 25-35, for example).

Cuny et al teach drug screening assays for identifying compounds with the ability to modulate receptors of interest, and also teach measurement of gene expression levels in response to a test compound wherein the amount of transcription is compared to transcription in the same cell in the absence of a test compound (see column 35, lines 36-50, column 36, lines 56-67 and column 37, lines 1-10, for example). Cuny et al disclose that a transcription-based assay is useful for identifying compounds that interact with any cell surface protein showing activity that alters gene expression (see lines 24-30, for example). Cuny et al do not teach that the effect of the EOI is analyzed by monitoring the EOI-induced modulation of a transcriptome.

MacLeod et al teach a method known as combinatorial oligonucleotide PCR (COP) for rapid analysis of gene expression changes in a transcriptome of a cell or tissue in response to treatment of a cell or organism with a pharmaceutical compound, (see column 7, lines 50-62, in particular). MacLeod et al disclose that said method has wide applications as a low cost screening tool to study changes in gene expression in about 90% of the transcriptome (see column 43, lines 39-42, and column 44, lines 21-24, for example).

It would have been obvious to one of ordinary skill in the art to modify the method of Cuny et al to use COP to monitor compound-induced modulation of a target cell transcriptome to identify a compound of interest for prevention or treatment of pain because Cuny et al teach that transcription changes in response to a test compound

can be measured using any method known to those of skill in the art (see column 36, lines 56-67, for example). MacLeod et al teach that the COP method of monitoring gene expression changes in a transcriptome of a cell or tissue in response to a compound or treatment is reliable, semi-quantitative and flexible. The motivation to do so is the expected benefit as suggested by Cuny et al and MacLeod et al of being able to rapidly and economically determine the effect of a test compound or EOI on modulation of gene expression to identify an EOI useful in the treatment of pain. There is reasonable expectation of success in using the COP method to identify EOI useful in the prevention or treatment of pain since it has worked before in the cited reference.

Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura McGillem, PhD
12/6/2005

DAVID GUZO
PRIMARY EXAMINER